REMARKS

Applicant appreciates the careful consideration given to this case by the Examiner. This application was originally filed with 20 claims. The Examiner has rejected claims 1-20. Applicant will address the issues raised in the Office Action in the order that they appear.

Applicant has amended the specification to properly include a claim of priority as a continuation-in-part application to U.S. Serial No. 08/923,813, filed on September 4, 1997, which issued as U.S. Patent No. 6,099,853 on August 8, 2000.

Claims 1-20 have been rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,099,853 ("the '853" patent). As noted above, Applicant has amended the subject application to make a claim of priority to U.S. Patent No. 6,099,853. Applicant includes herewith a "Terminal Disclaimer to Obviate a Double Patenting Rejection Over a Prior Patent" in order to obviate the Examiner's double patenting rejection, along with the appropriate fee. Based on the above, withdrawal of the double patenting rejection is hereby respectfully requested.

The Examiner has rejected claims 1-20 under 35 U.S.C. 112, first paragraph, arguing that the specification does not reasonably provide enablement for any and all antigens to be used in the suppository based delivery system. Applicant respectfully traverses this rejection, for the reasons set forth below, applicant believes the specification provides sufficient enablement for the claims as presented.

The Examiner states that the specification does not reasonably provide enablement for any and all antigens to be used in a suppository based delivery system. The specification reasonably provides enablement for certain adjuvants to be used (page 13, line 14) in accordance with a suppository based delivery system. Moreover, the types of vaccines that can be used in

accordance with the present invention can consist of pathogens from sources such as viral, bacterial, protozoan, or fungal pathogens (p. 10, line 11). The '853 patent claims a suppository-based vaccine delivery system that is comprised of inactivated bacteria which originate from cultures of 8 to 14 uropathogenic bacteria strains (column 5, line 25).

The Examiner states that the specification fails to teach how to formulate and use the claimed vaccines. However, the specification (page 11, line 1) teaches that the claimed vaccines may be formulated in a variety of ways. Moreover, the specification of the present application teaches how the claimed vaccines may be incorporated for use with the suppository base (page 13, line 14). Additionally, the '853 patent teaches how to formulate the vaccine in accordance with the present invention (Column 5, line 39). Therefore, there is support, both in the subject application and the '853 patent to which the subject application claims priority, for how to formulate and use the claimed vaccines.

The Examiner states that the specification does not provide substantive evidence that any antigen, in any amount, administered to any bodily orifice would be capable of inducing protective immunity. The specification provides substantive evidence that antigens administered through a anorectal or urogenital orifice are capable of inducing protective immunity. Applicant is not attempting to claim that any antigen, in any amount, can produce the intended result. The specification discloses that the vaccine or vaccine adjuvant(s) are comprised of whole or fractionated viral or other microbial pathogens, or their purified cellular constituents or derivatives, that consist of nucleic acids, proteins, lipids or other antigenic determinants capable of producing humoral- or cellular-mediated immunity (page 13, line 14). The '853 patent, by way of example and not limitation, provides evidence that the antigens administered in certain amounts are capable of preventing pathogenic infections in humans and animals (Column 8, line

5). Moreover, the example recites that in vivo protective immunity was achieved in subjects. Therefore, Applicant respectfully submits that Examiner's concerns have been addressed.

The Examiner states that the specification fails to teach the identity of cellular constituents, as well as how the cellular constituents can be mutated. The specification teaches the identity of the cellular constituents and how the cellular constituents can be mutated to induce protective immunity. Moreover, the specification provides an adequate written description of the antigens that would induce a vaccine effect. The specification discloses that the vaccine or vaccine adjuvant(s) are comprised of whole or fractionated viral or other microbial pathogens, or their purified cellular constituents or derivatives, that consist of nucleic acids, proteins, lipids or other antigenic determinants capable of producing humoral- or cellular-mediated immunity (page 13, line 14). Moreover, additional cellular constituents, surface antigens, or nucleic acid sequences are known to those skilled in the art.

The Examiner also indicates that a skilled artisan would be required to de novo locate, identify and characterize the claimed antigens. It is respectfully submitted that Applicant is not required to teach that which is well known in the art. 35 U.S.C. 112 requires that the specification be enabling only to one skilled in the art. Additionally, the specification need not disclose what is well-known to those skilled in the art, and already available to the public. Accordingly, a skilled artisan, without undue experimentation, would be able to identify and characterize the claimed antigens.

For these reasons, Applicant respectfully requests that the Examiner's rejection under 35 U.S.C. 112, first paragraph, be withdrawn.

The Examiner has rejected claims 1-20 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has suggested that the rejection of claims 1-20 can be obviated by amending the claims to remove the phrase "selected from the group consisting of." Accordingly, Applicant has amended the claims as provided above, with a version with markings to show changes made attached hereto. Applicant therefore, respectfully requests that this basis for rejection be withdrawn.

Examiner has requested clarification of the phrase "other antigenic determinants or combination thereof" (claims 1, 2, 3, 13, 14, 16). "Other antigenic determinants" refers to that which shares commonality in function with nucleic acids, proteins and lipids. "Combinations thereof" refers to combinations of nucleic acids, proteins, lipids and other antigenic determinants. Applicant therefore, respectfully requests that this basis for rejection be withdrawn.

Examiner has also requested clarification of the phrase "is generated from known genetic information" (claim 4). Claim 4 recites a claim to vaccine or vaccine adjuvants that are used as part of the suppository used to treat urogenital or anorectal tract infections. The type of vaccine or vaccine adjuvants to be used are determined based on the specific information of a particular pathogen. The "genetic information" is that which is specific to a pathogen. Applicant therefore, respectfully requests that this basis for rejection be withdrawn.

Examiner states that claim 13 recites the phrase "genetically engineered constituents of known pathogens selected from the group consisting of urogenital pathogens, anorectally

pathogens and combinations thereof." As filed, the application does not recite said phrase in claim 13. Applicant respectfully requests clarification as to this basis of rejection.

The Examiner states that claim 18 is confusing. Applicant has amended claim 18, and believes that such amendment addresses Examiner's rejection of said claim.

The Examiner has also made rejections based on 35 U.S.C. 102.

Applicant respectfully requests that, as there are no bases for rejections for claims 7-9, 12-13, and 18, subject to the 35 U.S.C. 112 rejection believed overcome herein, these claims should be allowable.

The Examiner rejected claims 1-4, 6-10, 14-15 and 17 under 35 U.S.C. § 102(b) as being anticipated by Uehling et al (June 1997). As noted above, Applicant has amended the subject application to make a claim of priority to the '853 patent. Accordingly, subject to the arguments presented therein and in connection herein with rejections based on 35 U.S.C. 112, Applicant respectfully submits that the Uehling reference is not a proper reference and that all claims are allowable.

The Uehling reference was the basis for an anticipatory and obviousness rejection in the parent application. Based upon the arguments and Declarations presented therein, the Uehling reference was found not to be a proper art reference, as summarized herein for the examiner's convenience.

Applicants responded to the use of the Uehling reference by filing executed Declarations presented by David T. Uehling, M.D., Zsolt I. Hertelendy, Pharm. D., Ph.D., and Murray Weiner, M.D. Among other statements, the Declarations verified that the formulation of the suppository-based vaccine delivery system of the present invention was only publicly disclosed with the permission of Drs. Hertelendy and Weiner and was first publicly disclosed in the June

1997 publication of Uehling et al., Vaginal Mucosal Immunization for Recurrent Urinary Tract Infection: Phase II Clinical Trial, *Journal of Urology*, 157:2049-2052, 1997. This public disclosure was made three months prior to the filing of the U.S. patent application, well within the 12 month statutory period regarding novelty.

The Declarations verified that the suppository-based vaccine delivery system of the present invention was not known or used by others, or patented or described in a printed publication before the invention thereof by applicants. Further, the Declarations verified that Dr. Uehling was not involved in the formulation, conception, or reduction to practice of the suppository-based vaccine delivery system of the present invention. Further, because the formulation of the suppository-based vaccine delivery system of the present invention was revealed to Dr. Uehling in April 1992 in confidence by Drs. Hertelendy and Weiner for the purposes of performing clinical testing, such a disclosure did not create a bar date. And finally, because the Uehling et al. article was published with the inventors' permission less than one year before the filing date of the application, the article could not be used as an art reference against the U.S. application.

Therefore, for the reasons identified above and presented in the parent application, Applicants believe use of the Uehling reference is improper and the objections based thereon should be withdrawn. Therefore, claims 10 and 11, not being subject to any further rejections, are now in condition for allowance.

As noted above, and for purposes for simplifying the issues presented herein, Applicant herein withdraws claims 14-16 from consideration, reserving the right to present these claims in any continuing application. Claim 17 is amended to include the limitations of claim 14, and arguments as to allowability are presented below.

Applicant has amended claims 1 and 17 to recite that rather than inserting the suppository into a "bodily orifice," the suppository is inserted into "an anorectal or urogenital orifice." The Beck reference teaches a method of inserting a suppository based delivery system through a bodily orifice in such a way that the suppository is contacted across the cervix and into the uterus. However, the present invention is directed toward bringing a suppository in contact with the tissue of the anorectal or urogenital orifices to allow transfer of the suppository material therethrough. There is no motivation or suggestion in the Beck patent, or the combination of Beck with Singh, Azria or Mizuno, to bring the suppository in contact with the anorectal or urogenital tissue. Accordingly, the claimed invention is not believed obvious in light of these references.

Based upon the amendments and arguments set forth above, this application is now believed to be in condition for allowance. Favorable action is requested.

Respectfully submitted,

BENESCH, FRIEDLANDER,
COPLAN & ARONOFF LLP

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Robert H. Earp, III
Reg. No. 41,004
2300 BP Tower
200 Public Square
Cleveland, OH 44114-2378
(216) 363-4642

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

(Amended) 1. A suppository based vaccine delivery system for prophylaxis against or treatment of urogenitally and anorectally transmitted infectious disease in humans and animals, said suppository comprising:

(a) a vaccine or vaccine adjuvant(s) **[selected from the group consisting]** of whole or fractionated viral or other microbial pathogens, or their purified cellular constituents, whether native, mutated, synthetic, cloned or recombinantly-expressed and combinations thereof, that consists of nucleic acids, proteins, lipids, other antigenic determinants or combinations thereof capable of producing humoral- or cellular-mediated immunity in humans or animals; and

(b) a suppository base, selected from the group consisting of polyethylene glycol, polysorbate and combinations thereof;

wherein the suppository is adapted to be inserted into a anorectal or urogenital **[bodily]** orifice of a human or animal so as to allow the suppository to be in contact with tissue of the anorectal or urogenital **[bodily]** orifice to facilitate transfer of suppository material therethrough.

(Amended) 2. A suppository based vaccine delivery system for prophylaxis against urogenital tract infections in humans, said suppository comprising:

(a) a vaccine or vaccine adjuvant(s) **[selected from the group consisting]** of whole or fractionated viral or other microbial pathogens, or their purified cellular constituents, whether native, mutated, synthetic, cloned or recombinantly-expressed and

combinations thereof, that consists of nucleic acids, proteins, lipids, other antigenic determinants or combinations thereof capable of producing humoral or cellular-mediated immunity in humans; and

(b) a suppository base, selected from the group consisting of polyethylene glycol, polysorbate and combinations thereof;

wherein the suppository is adapted to be inserted vaginally so as to allow the suppository to be in contact with vaginal mucous membrane to facilitate transfer of suppository material therethrough.

(Amended) 3. A suppository based vaccine delivery system for prophylaxis against anorectally transmitted infectious disease in humans or animals, said suppository comprising:

(a) a vaccine or vaccine adjuvant(s) **[selected from the group consisting]** of whole or fractionated viral or other microbial pathogens, or their purified cellular constituents, whether native, mutated, synthetic, cloned or recombinantly expressed and combinations thereof, that consists of nucleic acids, proteins, lipids, other antigenic determinants or combinations thereof capable of producing humoral or cellular-mediated immunity in humans or animals; and

(b) suppository base, selected from the group consisting of polyethylene glycol, polysorbate and combinations thereof;

wherein the suppository is adapted to be inserted rectally so as to allow the suppository to be in contact with the anorectal mucous membrane to facilitate transfer of vaccine or vaccine adjuvant material therethrough.

(Amended) 4. The suppository based vaccine delivery system of claim 1 wherein the vaccine content or vaccine adjuvant(s) is **[selected from the group consisting of]** whole cells, purified constituents or is generated from known genetic information of urogenital or anorectally transmittable pathogens.

(Amended) 12. A suppository-based vaccine delivery system for prophylaxis against urogenital or anorectally transmitted infections in humans or animals, said suppository comprising:

(a) a vaccine or vaccine adjuvant(s) comprising purified, mutated, synthetic or genetically engineered constituents of known pathogens **[selected from the group consisting]** of urogenital pathogens, anorectally pathogens and combinations thereof; and

(b) a suppository base, selected from the group consisting of polyethylene glycol, polysorbate and combinations thereof;

wherein the polyethylene glycol suppository base is comprised of about 75% to about 98% by weight polyethylene glycol and about 2% to about 25% by weight polysorbate, wherein the polyethylene glycol has an average molecular weight of about 950 to about 3700, and wherein the polyethylene glycol suppository base comprises from about 70% to about 99% by weight of the suppository; wherein the suppository is adapted to be inserted vaginally or rectally so as to allow the suppository to be in contact with mucous membrane to facilitate transfer of vaccine or vaccine adjuvant(s) material therethrough.

(Amended) 13. A suppository-based vaccine delivery system for prophylaxis against genitourinary or anorectal tract infections in humans or animals, said suppository resulting from the mixture of:

(a) a vaccine or vaccine adjuvant comprising **[selected from the group consisting of]** whole or fractionated viral or other microbial pathogens, or their purified cellular constituents, whether native, mutated, synthetic, cloned or recombinantly expressed, that consists of nucleic acids, proteins, lipids, other antigenic determinants or combinations thereof capable of producing humoral or cellular-mediated immunity in humans or animals; and

(b) a suppository base, selected from the group consisting of polyethylene glycol, polysorbate and combinations thereof;

wherein the polyethylene glycol suppository base is comprised of about 75% to about 98% by weight polyethylene glycol and about 2% to about 25% by weight polysorbate, wherein the polyethylene glycol has an average molecular weight of about 750 to about 3700, and wherein the polyethylene glycol suppository base comprises from about 70% to greater than 99% by weight of the suppository base; wherein the suppository is adapted to be inserted vaginally or rectally so as to allow the suppository to be in contact with mucous membrane to facilitate transfer of vaccine or vaccine adjuvant(s) material therethrough.

(Amended) 17. A method for producing an immune response in humans or animals, said method comprising the steps of **[of claim 14]**:

(a) inserting a suppository into an anorectal or urogenital orifice of a human or animal, wherein said suppository comprises a vaccine or vaccine adjuvant(s) material comprised of whole, fractionated viral or other microbial pathogens, or their purified cellular

constituents, whether native, mutated, synthetic, cloned or recombinantly expressed, that consists of nucleic acids, proteins, other antigenic determinants or combinations thereof capable of producing humoral or cellular-mediated immunity against urogenital or anorectal disease in humans or animals and a suppository base, wherein the **[polyethylene glycol]** suppository base is selected from the group consisting of polyethylene glycol, polysorbate and combination thereof; and

(b) contacting the suppository with mucosal tissue at and internal to the anorectal or urogenital orifice to facilitate transfer of the vaccine or vaccine adjuvant material therethrough and induce an immune response in the human or animal.

(Amended) 18. The method of claim 17 wherein the [polyethylene glycol] suppository base is comprised of about 75% to about 98% by weight polyethylene glycol and about 2% to about 25% by weight polysorbate.